In the Claims

Please replace all prior versions, and listings, of claims in the application with the following list of claims. Please amend claim 176 and cancel claims 47, 122, 143, 159, and 201 without prejudice or disclaimer.

1. (previously presented) In a method which calls for administration of interferon alpha (IFN-α) to a mammalian subject, the improvement comprising co-administering to the mammalian subject an effective amount of an isolated immunostimulatory nucleic acid, wherein said isolated immunostimulatory nucleic acid is 10 to 100 nucleotides long and comprises a poly-G sequence at each end and a central palindromic sequence comprising an unmethylated CpG dinucleotide.

2. (original) The improvement of claim 1, wherein the IFN-α is administered at a dose below the clinically established effective dose for IFN-α alone.

3. (original) The improvement of claim 1, wherein the IFN-α is administered at the maximum tolerated dose for IFN-α in the absence of the nucleic acid.

4. (original) The improvement of claim 1, wherein the IFN-α is administered at least 20 percent below the maximum tolerated dose of IFN-α in the subject.

5. (original) The improvement of claim 1, wherein the IFN-α is administered at least 30 percent below the maximum tolerated dose of IFN-α in the subject.

6. (original) The improvement of claim 1, wherein the IFN-α is administered at least 40 percent below the maximum tolerated dose of IFN-α in the subject.

7. (original) The improvement of claim 1, wherein the IFN-α is administered at least 50 percent below the maximum tolerated dose of IFN-α in the subject.

8. (previously presented) The improvement of claim 1, wherein the immunostimulatory nucleic acid is stabilized.

9. (original) The improvement of claim 1, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

10. (original) The improvement of claim 1, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

11.-17. (canceled)

18. (original) The improvement of claim 1, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

19. (previously presented) The improvement of claim 1, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGATCGTTGggggG	ODN 2252	SEQ ID NO:13
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACGTCGACGTggggG	ODN 2306	SEQ ID NO:30
ggGTCGTCGACGAgggggG	ODN 2329	SEQ ID NO:33
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

20. (original) The improvement of claim 1, further comprising co-administering GM-CSF to the subject.

21. (original) The improvement of claim 1, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

22. (original) The improvement of claim 1, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

23. (original) The improvement of claim 1, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

24. (previously presented) A method of supplementing interferon alpha (IFN-α) treatment of a subject, comprising

administering to a mammalian subject in need of IFN-α treatment an effective amount of IFN-α and an isolated immunostimulatory nucleic acid, wherein said isolated immunostimulatory nucleic acid is 10 to 100 nucleotides long and comprises a poly-G sequence at each end and a central palindromic sequence comprising an unmethylated CpG dinucleotide.

25.- 64. (canceled)

65. (previously presented) A method of increasing efficacy of interferon alpha (IFN-α) treatment of a subject, comprising:

administering to a mammalian subject in need of treatment with IFN-α a pharmaceutical composition comprising IFN-α, and

coadministering to the subject in need of such treatment a pharmaceutical composition comprising an immunostimulatory nucleic acid in an amount which, together with the administered IFN-α, is an effective IFN-α treatment, wherein the efficacy of the IFN-α treatment is greater than the efficacy of administering the same amount of IFN-α in the absence

of coadministering the immunostimulatory nucleic acid, and wherein said immunostimulatory nucleic acid is 10 to 100 nucleotides long and comprises a poly-G sequence at each end and a central palindromic sequence comprising an unmethylated CpG dinucleotide.

66.-81. (canceled)

82. (previously presented) A method of decreasing a dose of interferon alpha (IFN-α) effective for treating a subject, comprising:

administering to a mammalian subject in need of treatment with IFN-α a pharmaceutical composition comprising IFN-α, and

coadministering to the subject in need of such treatment a pharmaceutical composition comprising an immunostimulatory nucleic acid in an amount which, together with the administered IFN-α, is an effective IFN-α treatment, wherein the amount of administered IFN-α is less than an amount of IFN-α required in the absence of coadministering the immunostimulatory nucleic acid, and wherein said immunostimulatory nucleic acid is 10 to 100 nucleotides long and comprises a poly-G sequence at each end and a central palindromic sequence comprising an unmethylated CpG dinucleotide.

83.-102. (canceled)

103. (previously presented) A method of reducing an interferon alpha (IFN-α) treatment-related side effect in a subject receiving or in need of treatment with IFN-α, comprising

administering to a mammalian subject in need of treatment with IFN-α a pharmaceutical composition comprising IFN-α, and

coadministering to the subject in need of such treatment a pharmaceutical composition comprising an immunostimulatory nucleic acid in an amount which, together with the administered IFN-α, is an effective IFN-α treatment, wherein an IFN-α treatment-related side effect is reduced in comparison to the side effect when IFN-α is administered in the absence of coadministering the immunostimulatory nucleic acid, and wherein said immunostimulatory

nucleic acid is 10 to 100 nucleotides long and comprises a poly-G sequence at each end and a central palindromic sequence comprising an unmethylated CpG dinucleotide.

104.- 175. (canceled)

176. (currently amended) A method of stimulating production of a plurality of type I interferon (IFN) subtypes in a mammalian subject, comprising administering to a mammalian subject in need of IFN-α treatment an amount of immunostimulatory nucleic acid effective to induce IFN-producing cells (IPCs) to secrete at least two type I interferons, wherein said immunostimulatory nucleic acid is selected from the group consisting of

ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGATCGTTGgggggG	ODN 2252	SEQ ID NO:13
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACGTCGACGTggggG	ODN 2306	SEQ ID NO:30
ggGTCGTCGACGAgggggG	ODN 2329	SEQ ID NO:33
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

177.-201. (canceled)

202. (previously presented) A pharmaceutical composition, comprising

an isolated nucleic acid having a sequence selected from the group consisting of:

ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGATCGTTGgggggG	ODN 2252	SEQ ID NO:13
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACGTCGACGTggggG	ODN 2306	SEQ ID NO:30
ggGTCGTCGACGAgggggG	ODN 2329	SEQ ID NO:33
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage; and

a pharmaceutically acceptable carrier.

203. (previously presented) The pharmaceutical composition of claim 202, further comprising IFN-α.

204. (previously presented) The method of claim 1, wherein the co-administering comprises administering the IFN-α and the isolated immunostimulatory nucleic acid together.

205. (previously presented) The method of claim 1, wherein the co-administering comprises administering the IFN-α and the isolated immunostimulatory nucleic acid sequentially.

206. (previously presented) The method of claim 24, wherein the IFN-α is administered at a dose below a clinically established effective dose for IFN-α alone.

207. (previously presented) The method of claim 24, wherein the IFN-α is administered at a maximum tolerated dose for IFN-α in absence of the immunostimulatory nucleic acid.

208. (previously presented) The method of claim 24, wherein the IFN-α is administered at least 20 percent below a maximum tolerated dose of IFN-α in the subject.

209. (previously presented) The method of claim 24, wherein the IFN-α is administered at least 30 percent below a maximum tolerated dose of IFN-α in the subject.

210. (previously presented) The method of claim 24, wherein the IFN-α is administered at least 40 percent below a maximum tolerated dose of IFN-α in the subject.

211. (previously presented) The method of claim 24, wherein the IFN-α is administered at least 50 percent below a maximum tolerated dose of IFN-α in the subject.

212. (previously presented) The method of claim 24, wherein the immunostimulatory nucleic acid is stabilized.

213. (previously presented) The method of claim 24, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

214. (previously presented) The method of claim 24, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

215. (canceled)

216. (previously presented) The method of claim 24, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

217. (previously presented) The method of claim 24, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGATCGTTGggggG	ODN 2252	SEQ ID NO:13
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACGTCGACGTggggG	ODN 2306	SEQ ID NO:30
ggGTCGTCGACGAgggggggG	ODN 2329	SEQ ID NO:33
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

218. (previously presented) The method of claim 24, further comprising co-administering GM-CSF to the subject.

219. (previously presented) The method of claim 24, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

220. (previously presented) The method of claim 24, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

221. (previously presented) The method of claim 24, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

222. (previously presented) The method of claim 65, wherein the coadministering comprises administering the IFN-α and the immunostimulatory nucleic acid together.

223. (previously presented) The method of claim 65, wherein the coadministering comprises administering the IFN-α and the immunostimulatory nucleic acid sequentially.

224. (previously presented) The method of claim 65, wherein the pharmaceutical composition comprising an immunostimulatory nucleic acid is administered locally.

225. (previously presented) The method of claim 65, wherein the immunostimulatory nucleic acid is stabilized.

226. (previously presented) The method of claim 65, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

227. (previously presented) The method of claim 65, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

228. (canceled)

229. (previously presented) The method of claim 65, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

230. (previously presented) The method of claim 65, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGATCGTTGggggG	ODN 2252	SEQ ID NO:13
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACGTCGACGTggggG	ODN 2306	SEQ ID NO:30
ggGTCGTCGACGAgggggG	ODN 2329	SEQ ID NO:33
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

231. (previously presented) The method of claim 65, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

232. (previously presented) The method of claim 65, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

233. (previously presented) The method of claim 65, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

234. (previously presented) The method of claim 82, wherein the coadministering comprises administering the IFN-α and the immunostimulatory nucleic acid together.

235. (previously presented) The method of claim 82, wherein the coadministering comprises administering the IFN-α and the immunostimulatory nucleic acid sequentially.

236. (previously presented) The method of claim 82, wherein the amount of administered IFN-α is at least 20 percent below an amount of IFN-α required in absence of coadministering the immunostimulatory nucleic acid.

237. (previously presented) The method of claim 82, wherein the amount of administered IFN-α is at least 30 percent below an amount of IFN-α required in absence of coadministering the immunostimulatory nucleic acid.

238. (previously presented) The method of claim 82, wherein the amount of administered IFN-α is at least 40 percent below an amount of IFN-α required in absence of coadministering the immunostimulatory nucleic acid.

239. (previously presented) The method of claim 82, wherein the amount of administered IFN-α is at least 50 percent below an amount of IFN-α required in absence of coadministering the immunostimulatory nucleic acid.

240. (previously presented) The method of claim 82, wherein the pharmaceutical composition comprising an immunostimulatory nucleic acid is administered locally.

241. (previously presented) The method of claim 82, wherein the immunostimulatory nucleic acid is stabilized.

242. (previously presented) The method of claim 82, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

243. (previously presented) The method of claim 82, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

244. (canceled)

245. (previously presented) The method of claim 82, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

246. (previously presented) The method of claim 82, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGATCGTTGggggG	ODN 2252	SEQ ID NO:13
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACGTCGACGTggggG	ODN 2306	SEQ ID NO:30
ggGTCGTCGACGAgggggggG	ODN 2329	SEQ ID NO:33
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

247. (previously presented) The method of claim 82, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

248. (previously presented) The method of claim 82, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

249. (previously presented) The method of claim 82, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

250. (previously presented) The method of claim 103, wherein the co-administering comprises administering the IFN-α and the immunostimulatory nucleic acid together.

251. (previously presented) The method of claim 103, wherein the co-administering comprises administering the IFN-α and the immunostimulatory nucleic acid sequentially.

252. (previously presented) The method of claim 103, wherein the pharmaceutical composition comprising an immunostimulatory nucleic acid is administered locally.

253. (previously presented) The method of claim 103, wherein the IFN-α treatment-related side effect is systemic.

254. (previously presented) The method of claim 103, wherein the IFN-α treatment-related side effect is selected from the group consisting of flu-like syndrome, fever, headache, chills, myalgia, fatigue, anorexia, nausea, vomiting, diarrhea, and depression.

255. (previously presented) The method of claim 103, wherein the immunostimulatory nucleic acid is stabilized.

256. (previously presented) The method of claim 103, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected

from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

257. (previously presented) The method of claim 103, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

258. (canceled)

259. (previously presented) The method of claim 103, wherein the immunostimulatory nucleic acid is between 12 and 40 nucleotides in length.

260. (previously presented) The method of claim 103, wherein the immunostimulatory nucleic acid has a sequence selected from the group consisting of

ggGGGACGATCGTCgggggG	ODN 2216	SEQ ID NO:7
ggGGGACGATATCGTCgggggG	ODN 2245	SEQ ID NO:9
ggGGGACGAGCTCGTCgggggG	ODN 2247	SEQ ID NO:11
ggGGGACGATCGTTGggggG	ODN 2252	SEQ ID NO:13
ggGGTCACCGGTGAgggggG	ODN 2300	SEQ ID NO:24
ggGGTCGACGTACGTCGAgggggG	ODN 2301	SEQ ID NO:25
ggGGACGTCGACGTggggG	ODN 2306	SEQ ID NO:30
ggGTCGTCGACGAgggggG	ODN 2329	SEQ ID NO:33
ggGGTCGACGTCGACGTCGAGgggggG	ODN 2334	SEQ ID NO:36, and
ggGGACGACGTCGTGgggggG	ODN 2336	SEQ ID NO:37,

wherein each lower case letter represents phosphorothioate linkage and each upper case letter indicates phosphodiester linkage.

261. (previously presented) The method of claim 103, wherein the subject has a condition selected from the group consisting of a proliferative disorder and a viral infection.

262. (previously presented) The method of claim 103, wherein the subject has a proliferative disorder selected from the group consisting of: hairy cell leukemia, chronic myelogenous leukemia, cutaneous T-cell leukemia, multiple myeloma, follicular lymphoma, malignant melanoma, squamous cell carcinoma, AIDS-related Kaposi's sarcoma, renal cell carcinoma, prostate carcinoma, bladder cell carcinoma, cervical dysplasia, and colon carcinoma.

263. (previously presented) The method of claim 103, wherein the subject has a viral infection selected from the group consisting of: hepatitis B, hepatitis C, condyloma acuminatum, human immunodeficiency virus, herpes, cytomegalovirus, Epstein-Barr virus, and papillomavirus.

264. (canceled)

265. (canceled)

266. (previously presented) The method of claim 176, wherein the IPCs are precursor type 2 dendritic cells (pDC2s).

267. (canceled)

268. (previously presented) The method of claim 176, wherein the IPCs are induced to secrete at least three type I interferons.

269. (previously presented) The method of claim 176, wherein the IPCs are induced to secrete at least four type I interferons.

270. (previously presented) The method of claim 176, wherein the IPCs are induced to secrete at least five type I interferons.

271. (previously presented) The method of claim 176, wherein the IPCs are induced to secrete at least six type I interferons.

272. (previously presented) The method of claim 176, wherein the IPCs are induced to secrete at least seven type I interferons.

273. (previously presented) The method of claim 176, wherein the IPCs are induced to secrete at least eight type I interferons.

274. (previously presented) The method of claim 176, wherein the immunostimulatory nucleic acid is stabilized.

275. (previously presented) The method of claim 176, wherein the immunostimulatory nucleic acid comprises a backbone with at least one nuclease-resistant internucleotide linkage selected from the group consisting of: phosphorothioate, phosphorodithioate, methylphosphonate, and peptide.

276. (previously presented) The method of claim 176, wherein the immunostimulatory nucleic acid comprises at least one nucleotide analog or derivative.

Claims 277-280. (canceled)